REMARKS

Claims 1, 3, 5-8, 10-18, 22, 32, 34 and 35 were pending in this application. Claims 1, 14-15, 17 and 22 are currently amended without any intent of disclaiming equivalents thereof. The amendments to the claims introduce no new matter. Accordingly, upon entry of this paper, claims 1, 3, 5-8, 10-18, 22, 32, 34 and 35 will be pending and presented for consideration.

Claim Objections

Claims 14-15 and 17 were objected to for informalities. As suggested by the Examiner, Applicants have amended claims 14-15 and 17 by replacing "and" with "to", to clarify which of the recited members is present in the higher amount. Support for the amendments to claims 14-15, 17 can be found at least, for example, in the specification at paragraph 0042. Paragraph numbers used herein refer to the paragraph numbers of the published application.

Applicants submit that the amendments to claims 14-15 and 17 overcome the objection and respectfully request reconsideration and withdrawal of the objection.

Rejections under 35 U.S.C. § 112, First Paragraph

Claims 1, 3, 5-8, 10-18, 22, 32, and 34-35 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Specifically, the Office action alleges that recitation of the term "comprise" with respect to several claim elements introduces new matter into the application because the recited elements may include an unlimited number of additional components. The Office action alleges that the Applicants must provide support for each of these unlimited additional components in order to satisfy the written description requirement of 35 U.S.C. § 112, first paragraph. Applicants submit that the rejection is inappropriate and request reconsideration and withdrawal of the rejection.

First, the revised Written Description Training Materials promulgated by the U.S. Patent and Trademark Office illustrate that Applicants were in possession of the claimed invention. The Written Description Training Materials make clear that the disclosure of a single nucleic acid sequence sufficiently describes a claimed invention *comprising* that nucleic sequence

because other members of the genus would be predictable to one of skill in the art based on the disclosed structure of the nucleic acid. Example 4, Written Description Training Materials, Rev. 1, March 25, 2008. Similarly, Applicants' disclosure teaches and claims methods which include, among other things, proteins (e.g., C4BP and Protein S). A person of skill in the art would, consistent with the Written Description Training Materials, be able to readily predict and visualize other proteins which read on the claimed invention based on the teachings of Applicants' disclosure. Thus, even if, *arguendo*, Applicants' disclosure does not provide literal support for each of an unlimited additional components, Applicants would still fully satisfy the written description requirement because a person of skill in the art would consider Applicants to be in possession of a first member *comprising* protein S and a second member *comprising* C4b-binding protein (C4BP) or fragments thereof. For the above reasons, a person of skill in the art would also consider Applicants to be in possession of particles which *comprise* latex.

Second, the Office action attempts to distinguish Amgen, Inc. v. Hoechst Marion Roussel, Inc. on the grounds that Amgen involved product claims whereas Applicants' claims are process claims. 126 F.Supp.2d 69, 160 (D. Mass. 2001). Even if Amgen is so limited, which Applicants submit it is not, Applicants note that the claim language at issue here refers to *structural* elements of the claimed process. Applicants therefore submit that Amgen squarely applies to the claim language at issue, namely particles and proteins. Applicants further submit that the specification, figures and claims, as originally filed, provide sufficient description to enable one of skill in the art to make at least one mode of the claimed composition. For example, support for a particle comprising at least latex can be found at paragraphs [0054] and [0067]-[0069], and support for a first member comprising at least Protein S and a second binding member comprising at least C4BP can be found at paragraphs [0032], [0034], and [0063]. For example, paragraph [0063] of Applicants' published application states that "[b]inding members include, but are not limited to . . . proteins (e.g., protein S), . . . and fragments, conjugates, and/or derivatives thereof." Because Applicants have complied with the written description requirements and because one of skill in the art would consider Applicants to be in possession of the claimed invention, Applicants respectfully request reconsideration and withdrawal of the rejections.

Finally, claim 17 is rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing new matter. As noted above, Applicants have amended claim 17 to replace "between about 10 and 40" with "between about 10 to 40" to clarify which of the recited members is present in the higher amount. Applicants submit that the amendment to claim 17 overcomes the rejection. Applicants therefore respectfully request reconsideration and withdrawal of the rejection.

Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1 and 22 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

Without acquiescing to the rejection, and solely to advance prosecution, Applicants have amended claims 1 and 22 to further clarify the claimed subject matter. Applicants submit that the amendments overcome the rejections and respectfully request reconsideration and withdrawal of the rejections.

Non-statutory obviousness-type double patenting rejection

Claims 1, 3, 5-8, 10-17 are rejected as allegedly being unpatentable for non-statutory obviousness-type double patenting over claims 1-9 of U.S. Patent No. 6,379,975 in view of U.S. Patent No. 4,486,530 ("David").

Claims 1, 3, 5-8, 10-18, 22 and 34-35 are rejected as allegedly being unpatentable for non-statutory obviousness-type double patenting over claims 1-41 of U.S. Patent No. 7,041,458 in view of David.

Claim 32 is rejected as allegedly being unpatentable for non-statutory obviousness-type double patenting over claims 1-9 of U.S. Patent No. 6,379,975 in view of David, or alternatively over claims 1-41 of U.S. Patent No. 7,041,458 in view of Giri et al., Thomb. Haemost. 1998 Apr, 79(4):767-72 ("Giri").

Under 35 U.S.C. § 103(c), subject matter developed by another which qualifies as prior art only under 35 U.S.C. §§ 102(e), (f), or (g) will be considered owned by the same entity as an

application if a joint research agreement is properly asserted. Although assertion of a joint research agreement disqualifies the subject matter as prior art to the application, a double patenting rejection may still be proper. MPEP § 706.02(l)(III). Moreover, MPEP § 804(II)(B)(1) explains that, "the analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. 103 obviousness determination." Finally, if a joint research agreement is asserted and a double patenting rejection is deemed appropriate, the double patenting rejection can be overcome by filing a terminal disclaimer in the application. *See* 37 CFR § 1.321(d).

Here, the Office action alleges that a non-statutory double patenting rejection cannot be overcome by asserting a joint research agreement. However, Applicants asserted a joint research agreement not to overcome the double patenting rejection, but to show that this application and the referenced patents—U.S. Patent Nos. 6,379,975 and 7,041,458—should be considered commonly owned for the purposes of filing a terminal disclaimer. Applicants note that the double patenting rejection is a non-statutory obviousness-type double patenting rejection. Moreover, the patent references cited by the Office action are available as prior art only under 35 U.S.C. § 102(e). The Office action has therefore applied the same logic in rejecting the claims for a non-statutory obviousness-type double patenting rejection as would be used to reject the claims under 35 U.S.C. § 103. Therefore, Applicants should not be precluded from overcoming the double patenting rejection by asserting a joint research agreement and terminal disclaimer simply because the Office action rejected the claims for non-statutory obviousness-type double patenting straightaway rather than first rejecting the claims under 35 U.S.C. § 103.

Accordingly, Applicants submit that the application and U.S. Patent Nos. 6,379,975 and 7,041,458 are commonly owned, by virtue of the joint research agreement asserted in the response filed on January 24, 2008. Applicants therefore respectfully request that the double-patenting rejection be held in abeyance until such time that otherwise-allowable subject matter is acknowledged. At such time, Applicants will file an appropriate terminal disclaimer, in accordance with 37 C.F.R. § 1.321(d), over U.S. Patent Nos. 6,379,975 and 7,041,458 to obviate the double patenting rejection.

Rejection under 35 U.S.C. § 103: David in view of Giri

Claims 1, 3, 5-8, 10-12, 18, 22, 32, and 34 were rejected under 35 U.S.C. § 103(a) as being unpatentable over David in view of Giri. Applicants traverse the rejection to the extent it is maintained over the claims as amended.

David teaches the use of two monoclonal antibodies to form an antibody:antigen:antibody immunometric sandwich to detect the presence of an antigen. David neither teaches nor appreciates the use of a binding partner other than an antibody to detect an antigen in a two-site immunometric assay. Moreover, David does not teach or suggest that David's method may be used to detect an unbound form of a binding pair in a sample containing both the unbound form and a bound form of the first member.

Giri does not cure the deficiencies of David. Giri does not teach a method for detecting protein S using particles and detecting the formation of a second complex by measuring an increase in the turbidity of the sample. Instead, Giri teaches a direct enzyme-linked ligandsorbent assay (ELSA) using a binding member immobilized on a microtiter plate and requiring the further addition of a detectable substrate, for example, peroxidase, to identify isolated protein S. *See* Giri at pages 767-768, "Subjects, Materials and Methods." Additionally, the ELSA solid substrate assay taught by Giri is time consuming, difficult, and expensive to automate.

As discussed in Applicants' specification as originally filed at paragraphs [0009] and [0010], Giri does not teach or suggest that Giri's method may be used to detect an unbound form of a binding pair in a sample in the presence of both the unbound form and the bound form of the first member. Instead, Giri requires the separation of bound protein S (the bound form of the first member) from free protein S (the unbound form of the first member) either during the preanalytical step, by precipitation of bound protein S with polyethyleneglycol, or during the development of the immunoassay, by washing away the complex that does not bind to the solid phase. *See* Giri at page 768, left column.

Applicants submit that it would not have been obvious to combine the teachings of David and Giri to arrive at the claimed method. On the contrary, although David may suggest the use of monoclonal antibodies to detect a polyvalent antigen, David neither provides an invitation to

try binding partners other than monoclonal antibodies nor suggest how binding partners other than monoclonal antibodies might be used in David's method. Applicants submit that the Office action improperly focuses on the alleged obviousness of substitutions and differences, instead of looking at the combination of elements to result in *the invention as a whole*. *See* Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1382-83 (Fed. Cir. 1986).

Because the detection of unbound protein S provides one of the most valuable parameters for the clinical diagnosis of thrombotic disease, it is desirable to provide a rapid, low-cost, analyte detection method able to detect and quantitate the amount of unbound protein S in a sample which does not require separating bound from unbound forms of protein S. Accordingly, Applicants submit that Applicants' claimed method provides a solution to an unmet need in the market for automated thrombotic disease diagnostic assays and provides a commercial advantage over the method taught by Giri.

Applicants submit that neither David nor Giri, either alone or in combination, teach or suggest the claimed method. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Rejection under 35 U.S.C. § 103: David in view of Giri and Ballas

Claim 13 was rejected under 35 U.S.C. § 103(a) as being unpatentable over David in view of Giri and further in view of U.S. Patent No. 4,812,395 to Ballas et al. ("Ballas"). Applicants traverse the rejection to the extent it is maintained over the claims as amended.

David and Giri were discussed above with respect to amended independent claim 1, from which claim 13 depends. Ballas does not cure the deficiencies of David and Giri. Ballas does not teach or suggest an immunometric antigen detection method wherein at least one of the binding partners is a natural binding partner of the antigen, for example, C4BP or a fragment of C4BP that binds protein S.

Applicants submit that none of David, Giri, or Ballas, either alone or in combination, teach or suggest the claimed method. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Rejection under 35 U.S.C. § 103: David in view of Giri and Mischak

Claims 14-17 were rejected under 35 U.S.C. § 103(a) as being unpatentable over David in view of Giri and further in view of U.S. Patent No. 6,124,430 to Mischak *et al.* ("Mischak"). Applicants traverse the rejection to the extent it is maintained over the claims as amended.

David and Giri were discussed above with respect to amended independent claim 1, from which claims 14-17 depend. Mischak does not cure the deficiencies of David and Giri. Mischak does not teach or suggest an immunometric antigen detection method wherein at least one of the binding partners is a natural binding partner of the antigen, for example, C4BP or a fragment of C4BP that binds protein S.

Furthermore, with respect to claims 14 and 15, which specify the molar ratios of the two binding partners used in the claimed method, the second member (comprising C4BP or a fragment of C4BP that binds to protein S) and the third member (an antibody which specifically binds to the first member), Applicants submit that Mischak does not teach or suggest modifying the molar ratios of two *binding partners* used in the assay, as required by Applicants' amended claims 14 and 15.

Applicants submit that none of David, Giri, or Mischak, either alone or in combination, teach or suggest the claimed method. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

Rejection under 35 U.S.C. § 103: David in view of Giri and Cambiaso

Claim 35 was rejected under 35 U.S.C. §103(a) as being unpatentable over David in view of Giri in further view of U.S. Patent No. 4,184,849 to Cambiaso et al. ("Cambiaso"). Applicants traverse the rejection to the extent it is maintained over the claims as amended.

David and Giri were discussed above with respect to amended independent claim 1, from which claim 35 depends. Cambiaso does not cure the deficiencies of David and Giri. Cambiaso does not teach or suggest an immunometric antigen detection method wherein at least one of the binding partners is a natural binding partner of the antigen, for example, C4BP or a fragment of C4BP that binds protein S. Instead, Cambiaso teaches a mixed agglutination assay to detect the presence of antibodies or antigens in a liquid by mixing the liquid with first and second

particulate reagents which mutually agglutinate but whose agglutination is inhibited by the particular antibody or antigen in the liquid under assay. *See* Cambiaso at Abstract and columns 1 and 2.

Applicants submit that none of David, Giri or Cambiaso, either alone or in combination, teach or suggest the claimed method. Accordingly, Applicants respectfully request that this rejection be reconsidered and withdrawn.

CONCLUSION

Applicants believe that claims 1, 3, 5-8, 10-18, 22, 32, 34 and 35 are in condition for allowance. The Examiner is invited to telephone the undersigned attorney to discuss any remaining issues. Early and favorable actions are respectfully solicited.

Respectfully submitted,

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